FORM PTO-1390 REV. 2/01 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 05823.0194

U.S. APPLICATION NO. (If known, see 37CFR1.5): 09/786278

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/KR00/01171	October 18, 2000	October 18, 1999

TITLE OF INVENTION: METHOD FOR PREPARING CHIRAL ESTER

APPLICANT(S) FOR DO/EO/US: Jai Wook PARK; Mahn-Joo KIM; Jeong Hwan KOH; Hyun Min JUNG

Applicant(s) herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☐ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c)(2)).
   a. ☒ is attached hereto (required only if not communicated by the International Bureau).
   b. ☐ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed with the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371 (c)(2)).
   a. ☐ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154 (d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3)).
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☒ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. ☐ Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A Substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821-1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154 (d)(4).
19. ☐ A second copy of the English language translation of the international application 35 U.S.C. 154 (d)(4).
20. ☒ Other items or information:
   a. ☐ Copy of cover page of International Publication No. WO
   b. ☐ Copy of Notification of Missing Requirements.
   c. ☒ Copy of PCT Request.

JC02 Rec'd PCT/PTO 0 2 MAR 2001

U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 09/786278	INTERNATIONAL APPLICATION NO. PCT/KR00/01171	ATTORNEY'S DOCKET NUMBER 05823.0194

21. ☒ The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1000.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$860.00**

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search fee (37 CFR 1.445(a)(2)) paid to USPTO **$710.00**

International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$690.00**

International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33 (1)-(4) **$100.00**

	CALCULATIONS PTO USE ONLY	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$1000.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).	$	

CLAIMS	NUMBER FILED		NUMBER EXTRA	RATE		
Total Claims	11	- 20 =		x $18.00	$	
Independent Claims	1	-3 =		x $80.00	$	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)				+$270.00	$270.00	
TOTAL OF THE ABOVE CALCULATIONS =					$1270.00	
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by ½.					$	
SUBTOTAL =					$1270.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest priority date (37 CFR 1.492(f)).					$	
TOTAL NATIONAL FEE =					1270.00	
Fee for recording the enclosed assignment (37 CFR 1.21 (h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property. +					$40.00	
TOTAL FEES ENCLOSED =					$1310.00	
					Amount to be refunded:	$
					charged:	$

a. ☒ A check in the amount of $ 1310.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-0916. A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING**: Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P
1300 I Street, N.W.
Washington, D.C. 20005-3315

DATED: March 2, 2001

SIGNATURE
D. Patrick O'Reilley, Reg. 27,932
NAME/REGISTRATION NO.

METHOD FOR PREPARING CHIRAL ESTER

BACKGROUND OF THE INVENTION

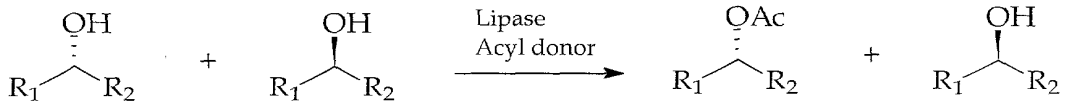
Field of the Invention

The present invention relates to a method for preparing a chiral ester and more particularly, the method for preparing an optically pure chiral ester from a ketone at a high yield by using an enzyme and a metallic catalyst.

It is one of important aims to convert a racemic mixture to an optically pure compound enantioselectively in organic synthesis. Recently, studies for using a metal or an enzyme as a catalyst have been increased in asymmetric syntheses. It has been widely known to use an enzyme as a catalyst for kinetic resolution of a racemic mixture in organic syntheses. A variety of effective methods for hydrolyses of esters and acylations of alcohols in the presence of lipase as a catalyst have been reported.

Kinetic resolution is the fact that the two enantiomers react at different rates with a chiral addend. An effective kinetic resolution is the enantioselective conversion from the racemic mixture to an optically pure product (scheme 1), leaving the other enantiomer in the reaction mixture.

Scheme 1



Conventional methods for preparing a chiral ester from a ketone such as asymmetric hydrogenation of an enol ester converted from a ketone, or esterification of a chrial alcohol prepared by asymmetric hydrogenation of a ketone require at least more than two step syntheses from a ketone to an enol

ester. These methods are relatively long and complicate.

SUMMARY OF THE INVENTION

Therefore, an object of the present invention is to provide a simple process for preparing an optically pure chiral ester at a high yield to resolve the above problems.

Detailed Description of the Invention

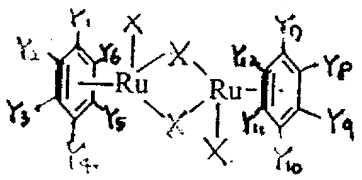
A process for preparing a chiral ester of the present invention is characterized by mixing and reacting: a ketone;

a ruthenium complex selected from the group consisting of compounds 1, 2 and 3 expressed in formulas 1 to 3 to activate hydrogenation of said ketone to a racemic alcohol and racemization of said racemic alcohol;

a lipase to acylate selectively one of enantiomers of said racemic alcohol;

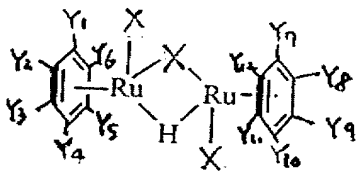
a hydride donor group to supply a hydride group to said ruthenium complex; and

an acyl donor group to supply acyl group to said lipase,



(1)

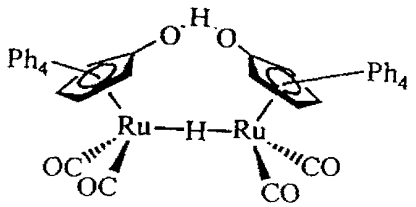
wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, Y_{10}, Y_{11}, and Y_{12} are independently a hydrogen atom or C_1-C_5 alkyl group; and X is Br, Cl or I;



(2)

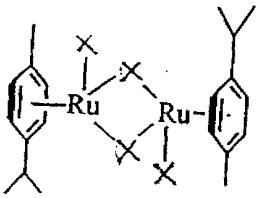
wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, Y_{10}, Y_{11}, and Y_{12} are independently a

hydrogen atom or C_1-C_5 alkyl group; and X is Br, Cl or I;



(3)

Said ruthenium complex is selected from the group consisting of the compounds 5 to 10 expressed in the following formulas 5 to 10,



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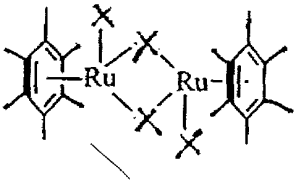

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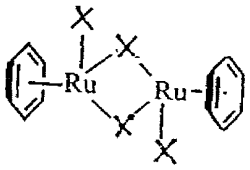

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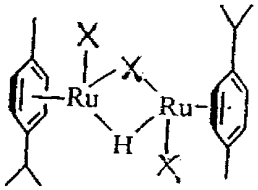

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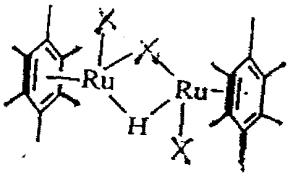

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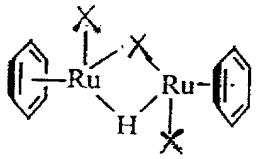


(10)

wherein X is Cl, Br or I, the most preferably Cl.

A method for preparing a chiral ester from a ketone through one-step synthesis is described in detail as set forth hereunder.

A mixture of a ruthenium complex selected from the group consisting of formulas 1 to 3, a lipase, a hydride donor, an acyl donor, and a ketone is reacted in an appropriate solvent in the presence of a base as shown in Scheme 2. The reaction condition can be varied with a structure of ruthenium complex. For example, when the ruthenium complex of formula 5 is used, the reaction is performed at a temperature of 40 to 50℃. When the ruthenium complex of formula 8 is used, the reaction requires 40 to 50℃ of a reaction temperature. When the ruthenium complex of formula 3 is used, the reaction requires 70 to 80℃ of a reaction temperature. The ruthenium complex of formula 5 is commercially available and can be converted to the ruthenium complex of formula 8 in alcohol/amine base condition. Therefore, results from the ruthenium complex of formula 5 and the ruthenium complex of formula 8 are almost same. A content of said ruthenium complex is preferred to use 0.1 to 5 mol%, relative to a ketone. If the content is more than 5 mol%, cost becomes expensive. On the other hand, if it is less than 0.1 mol%, the rate of the reaction becomes too slow.

Scheme 2

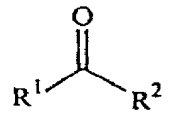
(4) (100)

wherein R^1, R^2 and R^3 are, independently, optionally substituted alkyl, optionally substituted aryl or optionally substituted cycloalkyl group and R^1 and R^2, R^1 and R^3, and R^2 and R^3 can be cyclized each other, where said substituent of alkyl, aryl and cycloalkyl is a hetero atom such as halogen atom and a cyano group.

Said ruthenium complex activates hydrogenation reaction of a ketone to a racemic alcohol by acting as a catalyst to transfer a hydrogen atom and further activates racemization of obtained racemic alcohol.

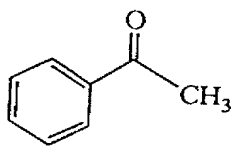
Said lipase, which is esterase, acylates one enantiomer from a racemic alcohol selectively to a chiral ester. Examples of lipase are *Pseudomonas cepacias* lipase and *Candida antarctica* lipase and more particulary, *Candida antarctica* component B lipase supported on acrylic resin (Novozym 435, Novo company) or *Pseudomonas cepacias* lipase supported on ceramic particle (lipase PS-C, Amano company), the most preferably *Candida antarctica* component B lipase supported on acrylic resin for heat resistance, reactivity, optical purity and the like. An amount of said lipase is in the range of 10 to 60mg, preferably 30 mg, relative to 1 mmol of a ketone in Novozym 435 case, and is in the range of 40 to 240 mg, preferably 80 mg, relative to 1 mmol of ketone in lipase PS-C case.

Said ketone is generally expressed in the formula 4. It is not limited but examples of the present invention are compounds 4a, 4b, 4c, 4d, 4e, 4f or 4g,

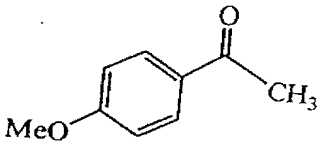


(4)

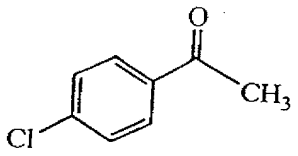
wherein R^1 and R^2 are the same as defined above.



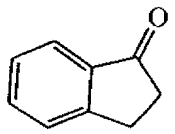
(4a)



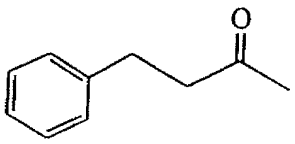
(4b)



(4c)



(4d)



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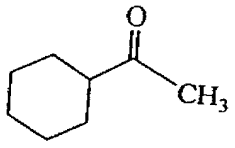
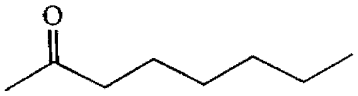


(4f)



(4g)

Said acyl donor supplies an acyl group to a lipase and acts to move a reaction balance to an acylated product in the presence of lipase catalyst. Preferred acyl donor is aryl ester or alkenyl acetate, the most preferably aryl ester such as *p*-chlorophenyl acetate having electron withdrawing group. An example of alkenyl acetate is isoprophenyl acetate. Such acyl donor compounds are preferred to use because they have an appropriate reactivity

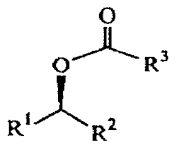
without inhibiting racemization. A preferred amount of said acyl donor compound is 2 to 4 equivalents to 1 equivalent of a ketone. If the amount is more than 4 equivalents to 1 equivalent of a ketone, it is difficult to isolate after reaction. On the other hand, if it is less than 2 equivalents to 1 equivalent of a ketone, the rate of acylation becomes too slow.

A hydride donor supplies a hydride to ruthenium complex. Examples of said hydride donor are 2,6-dimethylheptan-4-ol, hydrogen, and formic acid. Preferred amount of said hydride donor is 1 to 2 equivalents to 1 equivalent of ketone. If the content deviates from the range, it inhibits racemization reaction.

A base is also required to remove acid generated during the reaction. Said base includes triethylamine or diisopropylethyl amine and preferred amount to use is in the range of 1 to 2 equivalents to 1 equivalent to ketone.

Reaction solvent is not limited but it is preferred to use methylene chloride, toluene, benzene, or hexane because a solvent commonly affects production yield in enzymatic catalysis reaction. An amount of said solvent is used to be 0.2 to 0.3 M concentration of a ketone.

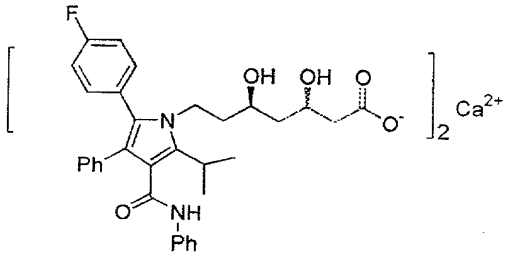
A chiral ester expressed in formula 100 is obtained by reacting a ketone, a ruthenium complex, a lipase, and an acyl donor compound in the presence of hydride donor,



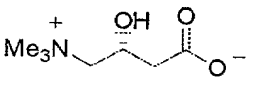
(100)

wherein R^1, R^2 and R^3 are, independently, optionally substituted alkyl, optionally substituted aryl or optionally substituted cycloalkyl group and R^1 and R^2, R^1 and R^3, and R^2 and R^3 can be cyclized each other, where said substituent of alkyl, aryl and cycloalkyl is a hetero atom such as a halogen atom and a cyano group.

The chiral ester of formula 100 of the present invention can be used as a synthetic intermediate for preparing various chiral compounds, chiral pharmaceutical drugs or chiral agrochemicals and more particularly, used as an essential intermediate for preparing Atorvastatin expressed in formula 101 which is a useful drug for treatment for hyperlipemia, L-Carnitine expressed in formula 102 which is as an additive used in food and drugs, and Agenerase expressed in formula 103 which is an essential intermediate of AIDS drug.



(101)



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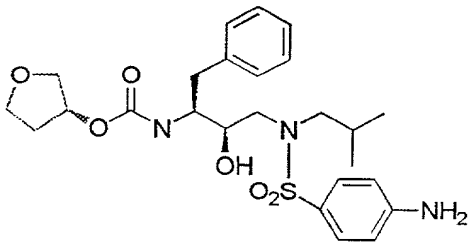
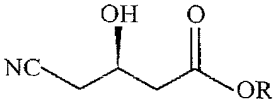


(103)

Especially, a chiral compound of formula 100a which is one of the compounds of the present invention is a key intermediate for preparing Atorvastatin of formula 101 disclosed in US Patent No. 5,908,953,



(100a)

wherein R is a low alkyl group.

The process for preparing a chiral ester of formula 100 of the present invention provides minimum production of by-products such as unreacted alcohol residue up to less than 5% and maximum production of product up to 100% having a high optical purity of 99% or more. Because optical purity is the most important factor in preparing chiral compounds for food and pharmaceutical drugs, the chiral ester of the present invention can be used as a useful starting material in various fields, especially fine chemical field.

The following examples are intended to be illustrative of the present invention and should not be construed as limiting the scope of this invention defined by the appended claims.

Example 1

A ketone of formula 4a(0.25mmol), triethylamine(0.75mmol), ruthenium complex of formula 5(0.0130mmol), where X is Cl, 2,6-dimethylheptan-4-ol(0.38mmol), and 20mg of lipase PS-C(Amano Company) were added to 2.0ml of methylene chloride. The reaction mixture was stirred for 5 min at room temperature and *p*-chlorophenyl acetate(0.75mmol) was added thereto to give a dark redish suspension.

Argon gas was purged into the reaction suspension, after removing an oxygen under the vacuum condition and then the suspension was heated at 50℃ for 78 hours.

Examples 2 to 5

The product, a chiral ester, was prepared by the same procedure of Example 1 except to use ketone of formulas 4b-4e instead of a ketone of formula 4a.

Example 6

The product, a chiral ester, was prepared by the same procedure of Example 1 except to use ruthenium complex of formula 8, where X is Cl, instead of the ruthenium complex of formula 5, where X is Cl.

Examples 7 to 10

The product, a chiral ester, was prepared by the same procedure of Example 6 except to use ketone of formulas 4b-4e instead of a ketone of formula 4a.

Example 11

A ketone of formula 4a(0.25mmol), ruthenium complex of formula 3(0.050mmol), 2,6-dimethylheptan-4-ol(0.38mmol), 7.5mg of Nozyme 435 and *p*-chlorophenyl acetate(0.75mmol) were added to 0.8ml of toluene to give a yellow suspension.

Argon gas was purged into the reaction suspension, after removing an oxygen under the vacuum condition and then the suspension was heated at 70℃ for 44 hours.

Examples 12 to 17

The product, a chiral ester, was prepared by the same procedure of Example 11 except to use ketone of formulas 4b-4g instead of a ketone of formula 4a.

In examples 1 to 5 and examples 11 to 17 to prepare chiral esters, formation of an alcohol as a by-product, yield of chiral acetates, and optical purity were determined and tabled in Table 1. Said yields of an alcohol and chiral acetate were analyzed by gas chromatography, and said optical purity

was determined by high performance liquid chromatography. Said gas chromatography used was Hewlett Packard 5890 Series II and said high performance liquid chromatography was SpectraSystem P2000.

Table 1

Section	Formation of alcohol (%)	Yield (%)	Optical purity (e.e.%)
Example 1	1	93	97
Example 2	0	81	99
Example 3	2	92	99
Example 4	0	73	99
Example 5	5	86	99
Example 11	2	96	98
Example 12	2	94	99
Example 13	2	98	99
Example 14	0	94	97
Example 15	0	100	99
Example 16	0	98	99
Example 17	0	95	95

As shown in Table 1, examples 1 to 5 and examples 11 to 17 proved that the present invention provides one-step synthesis for preparing an optically pure chiral ester form a ketone by controlling ruthenium complex to activate racemization and hydrogen transfer and lipase to activate esterification. Further, it provides high formation of the product, chiral ester, having less than 5% of unreacted alcohols.

CLAIMS

What is claimed is:

1. A process for preparing a chiral ester expressed in formula 100 of the present invention is characterized by mixing and reacting:

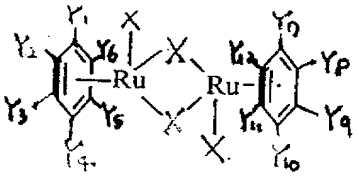
a ketone expressed in formula 4;

a ruthenium complex selected from the group consisting of compounds 1, 2 and 3 expressed in formulas 1 to 3 to activate hydrogenation of said ketone to a racemic alcohol and racemization of said racemic alcohol;

a lipase to acylate selectively one of enantiomers of said racemic alcohol;

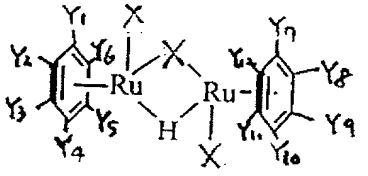
a hydride donor group to supply hydride group to said ruthenium complex; and

an acyl donor group to supply acyl group to said lipase,



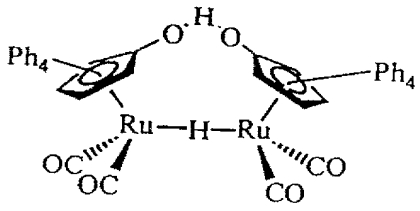
(1)

wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, Y_{10}, Y_{11}, and Y_{12} are independently a hydrogen atom or C_1-C_5 alkyl group; and X is Br, Cl or I;



(2)

wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, Y_{10}, Y_{11}, and Y_{12} are independently a hydrogen atom or C_1-C_5 alkyl group; and X is Br, Cl or I;



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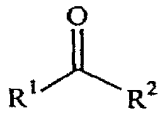

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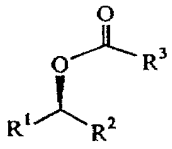
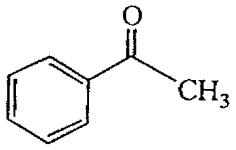


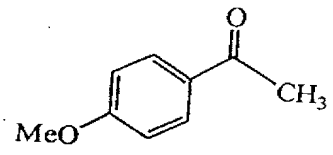
(100)

wherein R^1, R^2 and R^3 are, independently, optionally substituted alkyl, optionally substituted aryl or optionally substituted cycloalkyl group and R^1 and R^2, R^1 and R^3, and R^2 and R^3 can be cyclized each other, where said substituent of alkyl, aryl and cycloalkyl is a hetero atom such as a halogen atom and a cyano group.

2. The process for preparing a chiral ester according to claim 1, wherein said ketone is selected from the group consisting of the compounds 4a, 4b, 4c, 4d, 4e, 4f and 4g of formulas 4a to 4g.



(4a)



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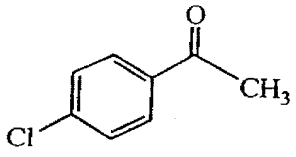
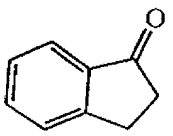
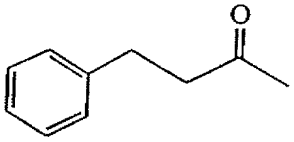


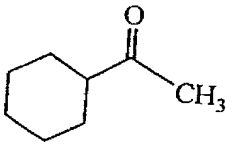
(4c)



(4d)



(4e)



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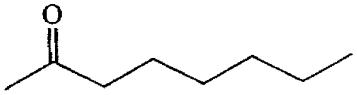
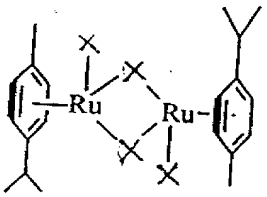


(4g)

3. The process for preparing a chiral ester according to claim 1, wherein said ruthenium complex is selected from the group consisting of compounds 5, 6, 7, 8, 9, and 10,



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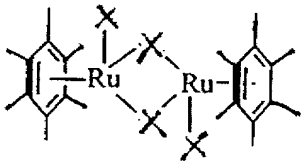

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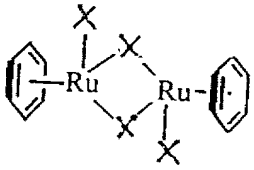

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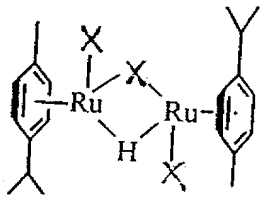

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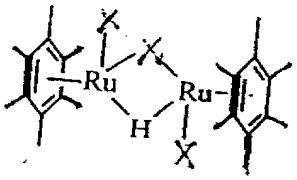

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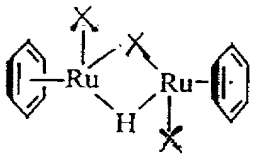


(10)

wherein X is Cl, Br or I.

4. The process for preparing a chiral ester according to any one of claim 1 to claim 3, wherein X is Cl.

5. The process for preparing a chiral ester according to claim 1, wherein said lipase is selected from the group consisting of *Pseudomonas cepacias* lipase and *Candida antarctica* component B lipase.

6. The process for preparing a chiral ester according to claim 1, wherein said acyl donor compound is aryl ester.

7. The process for preparing a chiral ester according to claim 6, wherein said aryl ester is selected from the group consisting of *p*-chlorophenyl acetate and alkenyl acetate.

8. The process for preparing a chiral ester according to claim 1, wherein said hydride donor compound is selected from the group consisting of 2,6-dimethylhepthan-4-ol, hydrogen and formic acid.

9. The process for preparing a chiral ester according to claim 1, wherein a content of said ruthenium complex is in the range of 0.1 to 5 mol%, relative to said ketone.

ABSTRACT

The present invention relates to a process for preparing a chiral ester expressed in formula 100 by mixing and reacting:

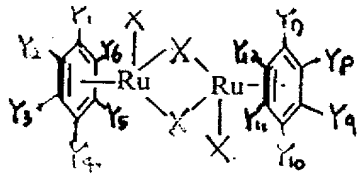
a ketone of formula 4;

a ruthenium complex selected from the group consisting of compounds 1, 2 and 3 expressed in formulas 1 to 3 to activate hydrogenation of said ketone to a racemic alcohol and racemization of said racemic alcohol;

a lipase to acylate selectively one of enantiomers of said racemic alcohol;

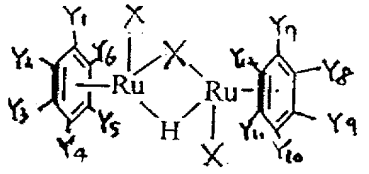
a hydride donor group to supply a hydride group to said ruthenium complex; and

an acyl donor group to supply acyl group to said lipase,



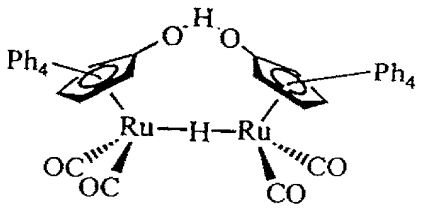
(1)

wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, Y_{10}, Y_{11}, and Y_{12} are independently a hydrogen atom or C_1-C_5 alkyl group; and X is Br, Cl or I;



(2)

wherein Y_1, Y_2, Y_3, Y_4, Y_5, Y_6, Y_7, Y_8, Y_9, Y_{10}, Y_{11}, and Y_{12} are independently a hydrogen atom or C_1-C_5 alkyl group; and X is Br, Cl or I;



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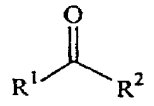

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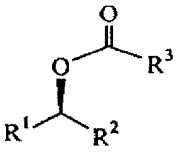

(100)

wherein R^1, R^2 and R^3 are, independently, optionally substituted alkyl, optionally substituted aryl or optionally substituted cycloalkyl group and R^1 and R^2, R^1 and R^3, and R^2 and R^3 can be cyclized each other, where said substituent of alkyl, aryl and cycloalkyl is a hetero atom such as a halogen atom and a cyano group.

Attorney Docket No.: _____

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; I believe I am the original, first, and sole inventor (if only one name is listed below) or an original, first, and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

METHOD FOR PREPARING CHIRAL ESTER

the specification of which:

is attached hereto; or

was filed as United States Application Serial No. _____
on _____, and was amended on _____
(if applicable) or

was filed as PCT International Application Number PCT/KR00/01171
on October 18, 2000, and was amended on _____
(if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate or § 365(a) of any PCT International application(s) designating at least one country other than the United States, listed below and have also identified below, any foreign application(s) for patent or inventor's certificate, or any PCT International application(s) having a filing date before that of the application(s) of which priority is claimed:

Country	Application Number	Date of Filing	Priority Claimed Under 35 U.S.C. 119	
Korea	99-45041	October 18, 1999	x YES	□ NO

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below:

Application Number	Date of Filing

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s) or § 365(c) of any PCT International application(s) designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior Unites States or PCT International application(s) in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application(s) and the national or PCT International filing date of this application:

Attorney Docket No.: _____

Application Number	Date of Filing	Status (Patented, Pending, Abandoned)

I hereby appoint the following attorney and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. **FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.**, Douglas B. Henderson, Reg. No. 20,291; Ford F. Farabow, Jr., Reg. No. 20,630; Arthur S. Garrett, Reg. No. 20,338; Donald R. Dunner, Reg. No. 19,073; Brian G. Brunsvold, Reg. No. 22,593; Tipton D. Jennings, IV, Reg. No. 20,645; Jerry D. Voight, Reg. No. 23,020; Laurence R. Hefter, Reg. No. 20,827; Kenneth E. Payne, Reg. No. 23,098; Herbert H. Mintz, Reg. No. 26,691; C. Larry O'Rourke, Reg. No. 26,014; Albert J. Santorelli, Reg. No. 22,610; Michael C. Elmer, Reg. No. 25,857; Richard H. Smith, Reg. No. 20,609; Stephen L. Peterson, Reg. No. 26,325; John M. Romary, Reg. No. 26,331; Bruce C. Zotter, Reg. No. 27,680; Dennis P. O'Reilley, Reg. No. 27,932; Allen M. Sokal, Reg. No. 26,695; Robert D. Bajefsky, Reg. No. 25,387; Richard L. Stroup, Reg. No. 28,487; David W. Hill, Reg. No., 28,220; Thomas L. Irving, Reg. No. 28, 619; Charles E. Lipsey, Reg. No. 28,165; Thomas W. Winland, Reg. No. 27,605; Basil J. Lewris, Reg. No. 28,818; Martin I. Fuchs, Reg. No. 28,508; E. Robert Yoches, Reg. No. 30,120; Barry W. Graham, Reg. No. 29,924; Susan Habeman Griffen, Reg. No. 30,907; Richard B. Racine, Reg. No. 30,415; Thomas H. Jenkins, Reg. No. 30,857; Robert E. Converse, Jr., Reg. No. 27,432; Clair X. Mullen, Jr., Reg. No. 20,348; Christopher P. Foley, Reg. No. 31,354; John C. Paul, Reg. No. 30,413; Roger D. Taylor, Reg. No. 28,992; David M. Kelly, Reg. No. 30,953; Kenneth J. Meyers, Reg. No. 25,146; Carol P. Einaudi, Reg. No.32,220; Walter Y. Boyd, Jr., Reg. No. 31,738; Steven M. Anzalone, Reg. No.32,095; Jean B. Fordis, Reg. No. 32,984; Barbara C. McCurdy, Reg. No. 32,120; James K. Hammond, Reg. No. 31,964; Richard V. Burgujian, Reg. No. 31,744; J. Michael Jakes, Reg. No. 32,824; Dirk D. Thomas, Reg. No. 32,600; Thomas W. Banks, Reg. No.32,719; Christopher P. Isaac, Reg. No. 32,616; Bryan C. Diner, Reg. No. 32,409; M. Paul Barker, Reg. No. 32,013; Andrew Chanho Sonu, Reg. No. 33,457; David S. Forman, Reg. No. 33,694; Vincent P. Kovalick, Reg. No. 32,867; James W. Edmonson, Reg. No. 33,871; Michael R. McGurk, Reg. No.32,045; Joann M. Neth, Reg. No. 36,363; Gerson S. Panitch, Reg. No. 33,751; Cheri M. Taylor, Reg. No. 33,216; Charles E. Van Horn, Reg. No. 40,266; and Linda A. Wadler, Reg. No. 33,218; and _____.
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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

ATTORNEY DOCKET NO.: _____

IN TESTIMONY WHEREOF, I/We have hereunto set our hand(s).

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Signature: Jung. H. M.

Date : Nov. 9. 2000

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.